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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LUKTON, DAVID	
ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/20/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/202,359	Arad
Examiner	**Art Unit**
David Lukton	1653

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Sep 24, 2001*

2a) ☐ This action is **FINAL.** 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *1-17 and 19* is/are pending in the applica

4a) Of the above, claim(s) *1-7 and 9-11* is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *8, 12-17, and 19* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
18) ☐ Interview Summary (PTO-413) Paper No(s) _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other

Pursuant to the directives of paper No. 21 (filed 9/24/01), claims 8, 12-17, 19 have been amended, and claim 18 cancelled. Claims 1-17 and 19 remain pending, of which 1-7, 9-11 remain withdrawn from consideration. Claims 8, 12-17, 19 are examined in this Office action.

Applicants' arguments filed 9/24/01 have been considered and found persuasive in part. The rejection over Baratz ('941) is withdrawn.

*

Figure 2A is objected to.

- In each of the first two structures, there is phenyl ring with a hydroxyl group bonded to it. In each of these structures, the oxygen atom should be adjacent to the phenyl ring, rather than the hydrogen atom.
- On the second page of figure 2A, the following phrase is present: "or any branched a**lyp**hatic chain". Here, the term "a**lyp**hatic" is misspelled.
- Also, on the second page of figure 2A, the following phrase is present:

  "R"' = small or branched aliphatic like side chain of Leu Val Ile **o** "

  What is the purpose of the letter "o" that follows "Ile"...?
- Also, on the second page of figure 2A, the last structure contains the following side chain moiety:

$(CH_2)_4$-N-C$(NH_2)_2$

It appears that a guanidino group is intended (i.e., the side chain of arginine). If so, the nitrogen and carbon atoms should be double -bonded to one another.

- On the third page of figure 2A, the word "etc." appears several times. How should one interpret this? It is suggested that the word "etc." be deleted.
- In addition to the foregoing, a new figure legend will be required, since a given figure should be limited to one page.

*

Claims 8, 12, 17, 19 (submitted on or after 8/15/00) are drawn to several inventions, at least one of which is directed to an invention that is independent or distinct from the invention originally claimed. In the claims as originally filed, variable "Z" (not Z') could not represent hydrogen. Now, the claims include this possibility. Compounds in which a hydroxyl group is *ortho-* to the "X" moiety are regarded as distinct from those in which only a hydrogen atom is present. Moreover, the volume of literature that discloses compounds in which only a hydrogen atom is present *ortho* to a carbonyl (or sulfoxide) is much greater than the volume of literature disclosing compounds having a hydroxyl group at this position. The biochemical properties will differ, and different searches will be required. In addition, claims which encompass the possibility of Y' being hydroxyl are regarded as encompassing non-elected subject matter.

Since applicant has received an action on the merits for the originally presented invention,

this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, embodiments in which "Z" is hydrogen are regarded as non-elected, as are those in which Y' is hydroxyl. (See 37 C.F.R. § 1.142(b) and M.P.E.P. § 821.03).

*

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8, 12-17, 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As indicated previously, the claims encompass a process in which neither the time nor the conditions are effective to inhibit replication of a picornavirus. In response, applicants have argued that a potential practioner can attempt to glean from the disclosure that which may be intended. Perhaps this is true, but that is not the issue. The issue is that the claims encompass processes in which neither the time nor the conditions are effective to inhibit replication of a picornavirus. If the time period of administration is not sufficient to achieve inhibition, then how can inhibition be achieved? Either or both of the following can be used:

A method of inhibiting replication of a picornavirus comprising administering to a subject in need thereof a compound of the formula ...
... for a time and under conditions effective to inhibit replication of said picornavirus.

A method of inhibiting replication of a picornavirus comprising contacting the picornavirus with a compound of the formula ... ... for a time and under conditions effective to inhibit replication of said picornavirus.

*

Claims 8, 12-17, 19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

- In each of claims 13-16, a narrow subgenus has been extracted out from the large genus originally disclosed. However, this amounts to new matter. If applicants believe that support exists for the recited subgenera, applicants should point out the relevant page and line numbers.

- In the specification (including the claims) as originally filed, variable "Z" could not represent hydrogen. This is evident from the description on page 5, as well as the various subgenera depicted on pages 6-10. Thus, there was no description of a genus in which "Z" could represent hydrogen. (In the event that applicants can identify only a single specie in which "Z" is hydrogen, this will not amount to a description of a genus).

- As indicated in the previous Office action, in at least one of the claims (claim 8), it is recited that substituent variables Y and Y' can be hydroxyl. It does not appear that there is support in the specification for this. In response, applicants have argued that in "previous claims" 8 and 18, there was a recitation that Y and Y' can be hydroxyl. While it may be true that in claims amended or added after filing, there was a recitation that Y and Y' can be hydroxyl, but this does not in any way amount to descriptive support for the claimed invention. What matters is what was present at the time of filing. In addition, applicants have pointed to page 30, where there

is indeed a recitation of a single compound in which Y' could be hydroxyl. However, all that is present is descriptive support for a single compound in which Y' is hydroxyl *at the same time* that R_3 is hydrogen, *at the same time* that Y is hydrogen, *at the same time* that Z' is hydrogen, *at the same time* that "X" is carbonyl, and *at the same time* that R_1 is methyl. Applicants may add a claim to a method of using such a compound, if deemed appropriate. However, recitation of a single compound is not tantamount to description of a genus. Applicants have also noted that original claim 5 recited that Y' could be hydroxyl. But the following two limitations are present in original claim 5. First, the claim is drawn to a group of compounds, i.e., the claim is drawn to compounds *per se*, not to a method of use. Second, the group of compounds identified in claim 5 constitutes a very narrow subgenus of the total. Thus, were it the case that applicants were claiming compounds *per se* (rather than a method of use), then applicants could claim exactly what is recited in claim 5. However, the question of what applicants might want to claim in another application is moot at the present time. The rejection is maintained.

- The claims encompass a process in which neither the time nor the conditions are effective to inhibit replication of a picornavirus. However, the specification does not explain how to use the compounds if neither the time period of administration is not sufficient, or if the conditions are not effective for this purpose. In addition, several of the claims do not require administration of the compounds to a subject. If the compounds are administered to a test tube, how does the infected patient benefit?

*

Claims 8, 12-17, 19 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 8 recites the following:

  "A method of inhibiting picornaviral replication in a subject comprising ... administering an effective amount of a compound... .... to effectively inhibit picornaviral replication".

That is, after stripping out formula I and the substituent variable definitions, one is left with the following phrase:

"...administering an effective amount of a compound... to effectively inhibit picornaviral replication".

Apart from the substantive issues, this language is objectionable because of the redundant use of the term "effective".

- Claims 13-15, 17, 19 are indefinite as to the process steps, and indefinite as to whether the compound is actually administered to the subject or not. If the compound is added to a test tube, is that sufficient to achieve inhibition of the replication in a human? In addition, the claims are indefinite as to whether the time of administration, conditions are effective to inhibit replication of a picornavirus.

  Either or both of the following can be used:

  A method of inhibiting replication of a picornavirus comprising administering to a subject in need thereof a compound of the formula ...
  ... for a time and under conditions effective to inhibit replication of said picornavirus.

  A method of inhibiting replication of a picornavirus comprising contacting the picornavirus with a compound of the formula ... ... for a time and under conditions effective to inhibit replication of said picornavirus.

- In claim 12, the phrase "the picornavirus species" lacks antecedent basis.

- In each of claims 15-16, it is recited that R1 can be the following: -CFCF-Phenyl

  However, in this structure, the carbon atoms bearing fluorine are trivalent, which is an error unless the carbon atoms are sp2-hybridized. Either of the following can be used:

  -CF=CF-Phenyl

- or -
-CHF-CHF-Phenyl

- In each of claims 13 and 14, there is a mandate that "X" must be carbonyl, and that R_1 must be trifluoromethyl. There are no other options for these variables. Accordingly, the proviso ("except when X-R_1 is a fluorinated ketoacyl group...") is superfluous and should be eliminated.

- Each of claims 8, 17, 19 recite that Y and Y' can be keto, carbamido, sulfoxide or alkylsulfonyl sulfone. However, each of these functional groups must be bonded to two other groups; only one of these is accounted for. Accordingly, the claims are rendered indefinite. A ketone, for example, is a carbonyl group that is is bonded to two other groups. In the case of, e.g.., claim 8, what other group can the carbonyl be bonded to.... an alkyl group, an alkaryl group, a heterocyclic group... what are the options? In response, applicants have pointed to *Ex part Altermatt* (183 USPQ 436, 1974), which pertained to US Patent 3,838,145. However, this case is not especially relevant. First, the terms at issue apply to bivalent moieties, i.e., moieties that must be bonded to two different groups. Second, in the *Altermatt* case, the moietes which could bond to the divalent groups (e.g., alkylene) were defined. By contrast, there is no suggestion in the claims as to what the keto, carbamido, sulfoxide or sulfone can be bonded to. The rejection is maintained.

*

The following is a quotation of the appropriate paragraphs of 35 U.S.C §102 that form the basis for the rejections under this section made in this action.

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 8, 17, 19 are rejected under 35 U.S.C. §102(b) as being anticipated by Berger (USP 3,657,436).

As indicated previously, Berger teaches (col 2, line 7) that the compounds disclosed in col 1, line 34+ can be used to treat a disease caused by a picornavirus. In response, applicants have amended the claims the eliminate the possibility of "Z" being amino. However, variable Z' can still be amino; thus, the anthranilic acid (2-amino-benzoic acid) core structure is still encompassed by the claims. The rejection is maintained.

*

Claim 8, 12, 17, 19 are rejected under 35 U.S.C. §102(b) as being anticipated by Singh (*Tetrahedron Letters* **32**, 5279, 1991).

Singh teaches (p. 5280) the compound thysanone, which inhibits rhinovirus. This corresponds to applicants variables as follows:

Z = H
Y = OH
Y' = OH
R3 = H
Z' and R_1 form a ring

Applicants have responded by arguing that their substituent variable R_{11} cannot form a ring. However, there was never an assertion by the examiner that R_{11} could form a ring; this rejection does not require such. Instead, the rejection is predicated on the fact that the instant claims encompass the possibility that variable Z', taken together with R_1 can form a ring. In other words, the description of what Z' and R_1 can be combined to form supercedes any description of R_{11}.

The rejection is maintained.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton [phone number (703)308-3213].

An inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

DAVID LUKTON
PATENT EXAMINER
GROUP 1800